

WHAT IS CLAIMED IS:

1. A method of inhibiting addiction-related behavior in a subject suffering from cocaine addiction, the method comprising administering to the subject a therapeutically effective amount of a therapeutic agent which has the ability to modulate the level of activity of a polypeptide encoded by at least one gene identified in one or more of Tables 1-15.

2. The method of claim 1, wherein the therapeutic agent modulates the level of transcription or translation of the gene.

3. The method of claim 1, wherein the therapeutic agent modulates the enzymatic activity of a polypeptide encoded by the gene.

4. The method of claim 1, wherein the gene is identified in one or more of Tables 1, 5, 8, 11 and 14.

5. The method of claim 1, wherein the gene is identified in Table 1.

6. The method of claim 5, wherein the at least one gene identified in Table 1 encodes a polypeptide selected from the group consisting of GABA-B receptor subunit gb2, myelin-associated basic protein, calcitonin receptor, Bos taurus-like neuronal axonal protein, FRA-2, similar to human oxygen-regulated protein, similar to mouse mrg 1 protein, pentraxin, olfactomedin-related protein, arc-growth factor enriched in dendrites, protein tyrosine phosphatase, melanocortin 4 receptor, ALK-7 kinase, neuritin and CB1 cannabinoid receptor.

7. The method of claim 6, wherein the polypeptide is GABA-B receptor subunit gb2, FRA-2 or CB1 cannabinoid receptor.

8. The method of claim 1, wherein the gene is identified in Table 2.

9. The method of claim 1, wherein the gene is identified in Table 4.

10. The method of claim 9, wherein the gene identified in Table 4 encodes a polypeptide selected from the group consisting of GABAB receptor 1d, tyrosine kinase receptor RET and Neurodap-1.

11. The method of claim 1, wherein the gene is identified in Table 5.

12. The method of claim 11, wherein the gene identified in Table 5 encodes a polypeptide selected from the group consisting of inhibin alpha-subunit and vesicular transport factor.

13. The method of claim 1, wherein the gene is identified in Table 6.

14. The method of claim 13, wherein the gene identified in Table 6 encodes a polypeptide selected from the group consisting of GABAB receptor 1c and phosphatidylinositol 4-kinase.

15. The method of claim 1, wherein the gene is identified in Table 7.

16. The method of claim 15, wherein the gene identified in Table 7 encodes a polypeptide selected from the group consisting of somatostatin-14 and kainate receptor subunit (ka2).

17. The method of claim 1, wherein the at least one gene is identified in Table 8.

18. The method of claim 17, wherein the at least one gene identified in Table 8 encodes a polypeptide selected from the group consisting of melanocortin-3 receptor, somatostatin, metabotropic glutamate receptor 3, NCAM polypeptide and synaptic SAPAP-interacting protein.

19. The method of claim 1, wherein the at least one gene is identified in Table 9.

20. The method of claim 19, wherein the at least one gene identified in Table 9 is calpastatin.

21. The method of claim 1, wherein the at least one gene is identified in Table 10.

22. The method of claim 21, wherein the at least one gene identified in Table 10 encodes a polypeptide selected from the group consisting of RAC protein kinase alpha, alpha-2B-adrenergic receptor and SNAP-25A.

23. The method of claim 1, wherein the at least one gene is identified in Table 11.

24. The method of claim 23, wherein the at least one gene identified in Table 11 encodes a polypeptide selected from the group consisting of oxytocin/neurophysin, NMDAR2C and GABA-A receptor epsilon.

25. The method of claim 1, wherein the at least one gene is identified in Table 12.

26. The method of claim 25, wherein the at least one gene identified in Table 12 encodes a polypeptide selected from the group consisting of phosphodiesterase I, tyrosine phosphatase and dopamine transporter.

27. The method of claim 1, wherein the at least one gene is identified in Table 13.

28. The method of claim 27, wherein the at least one gene identified in Table 13 encodes synaptotagmin IV homolog.

29. The method of claim 1, wherein the at least one gene is identified in Table 14.

30. The method of claim 29, wherein the at least one gene identified in Table 14 encodes a polypeptide selected from the group consisting of calmodulin, protein kinase rMNK2 and phospholipase C-beta1b.

31. The method of claim 1, wherein the at least one gene is identified in Table 15.

32. The method of claim 31, wherein the at least one gene identified in Table 15 encodes a polypeptide selected from the group consisting of phosphatidylinositol 4-kinase and protein-tyrosine-phosphatase.

33. The method of claim 1, wherein the therapeutic agent is selected from the group consisting of an antisense sequence, a ribozyme, a double stranded RNA, an antagonist and an agonist.

34. The method of claim 1, wherein the cocaine-addiction related behavior is cocaine seeking.

35. A method of inhibiting addiction-related behavior in a subject suffering from cocaine addiction, the method comprising administering to the subject a therapeutically effective amount of a therapeutic agent which has the ability to decrease transcription/translation of, or decrease the activity of a protein encoded by, at least one gene that encodes a polypeptide selected from the group consisting of hypertension-regulated vascular factor, myelin-associated basic protein, PB cadherin, calcitonin receptor, melanocortin 4 receptor, ALK-7 kinase, and retroposon.

36. The method of claim 35, wherein the therapeutic agent is selected from the group consisting of an antisense sequence, a ribozyme, a double stranded RNA, an antagonist and an agonist.

37. A method of inhibiting addiction-related behavior in a subject suffering from cocaine addiction, the method comprising administering to the subject a therapeutically effective amount of an agonist that activates a protein selected from the group consisting of

GABA-B receptor subunit gb2, cell adhesion-like molecule, bos taurus-like neuronal axonal protein, a polypeptide similar to mouse chemokine-like factor, FRA-2, a protein similar to human oxygen-regulated protein, a protein similar to mouse mrg1 protein, pentraxin, malic enzyme, olfactomedin-related protein, arc-growth factor, protein tyrosine phosphatase, krox, neuritin, microtubule-associated protein 2d, and CB1 cannabinoid receptor.

38. A method for identifying an agent to be tested for an ability to prevent or inhibit cocaine addiction-related behavior, the method comprising:

- a) combining in a reaction mixture a candidate agent with a protein encoded by a gene identified in Tables 1-15; and
- b) determining whether the candidate agent binds to and/or modulates activity of the protein.

39. The method of claim 38, wherein the protein is selected from the group consisting of hypertension-regulated vascular factor, myelin-associated basic protein, PB cadherin, calcitonin receptor, ALK-7 kinase and retroposon, cell adhesion-like molecule, bos taurus-like neuronal axonal protein, a polypeptide similar to mouse chemokine-like factor, FRA-2, a polypeptide similar to human oxygen-regulated protein, a polypeptide similar to mouse mrg1 protein, pentraxin, malic enzyme, olfactomedin-related protein, arc-growth factor, protein tyrosine phosphatase, krox, neuritin and microtubule-associated protein.

40. The method of claim 38, further comprising adding to the reaction mixture a competitor molecule that competes with binding of the candidate agent to the protein, either prior to or subsequent to combining the protein with the candidate agent.

41. The method of claim 38, wherein the reaction mixture is a cell-free protein mixture.

42. The method of claim 38, wherein the reaction mixture comprises a cell membrane preparation.

43. The method of claim 38, wherein the reaction mixture comprises a cell that comprises a heterologous gene that encodes the protein.

44. The method of claim 38, wherein (b) comprises determining a change in the level of an intracellular second messenger responsive to signaling by the protein.

45. The method of claim 38, wherein (b) comprises detecting a change in the level of expression of a reporter gene operatively linked to a transcriptional control sequence.

46. The method of claim 45, wherein the reporter gene encodes a protein selected from the group consisting of luciferase, alkaline phosphatase, chloramphenicol acetyl transferase and β -galactosidase.

47. The method of claim 38, wherein the method further comprises:

c) administering the candidate agent identified in b) to a cocaine-addicted subject or brain cells of a cocaine-addicted subject, wherein the cocaine-addicted subject is undergoing withdrawal; and

d) determining a level of expression of at least one gene identified in Tables 1-15 in brain cells of the cocaine-addicted subject, and comparing the level of expression to that observed in brain cells of a cocaine-addicted subject to which the candidate agent is not administered, wherein a change in expression level is indicative of the candidate having efficacy in preventing or inhibiting cocaine addiction-related behavior.

48. The method of claim 38, wherein the method further comprises:

c) administering the candidate agent identified in b) to a cocaine-addicted subject that is undergoing withdrawal; and

d) determining whether the withdrawal symptoms exhibited by the subject are reduced upon administration of the candidate agent.

49. A method for identifying an agent to be tested for an ability to prevent or inhibit addiction related behavior, the method comprising:

a) exposing a cocaine-addicted subject or brain cells of a cocaine-addicted subject to a candidate agent, wherein the cocaine-addicted subject is undergoing withdrawal;

b) determining a level of expression of at least one gene in the cocaine-addicted subject or brain cells of the cocaine-addicted subject, wherein the at least one gene is identified in Tables 1-15; and

c) comparing the level of expression of the gene in the cocaine-addicted subject or brain cells of the cocaine-addicted subject in the presence of the candidate agent with the level of expression of the gene in the cocaine-addicted subject or brain cells of the cocaine-addicted subject in the absence of the candidate agent, wherein a reversal in the level of expression of the gene in cocaine-addicted subject or brain cells of the cocaine addicted subject in the presence of the candidate agent relative to the level of expression of the gene in the absence of the candidate agent indicates that the candidate agent is an agent to be tested for the ability to prevent or inhibit addiction related behavior.

50. The method of claim 49, wherein the at least one gene is identified in Tables 1, 5, 8, 11 and 14.

51. The method of claim 49, wherein the at least one gene is identified in Table 1.

52. The method of claim 51, wherein the at least one gene identified in Table 1 encodes a polypeptide selected from the group consisting of GABA-B receptor subunit gb2, myelin-associated basic protein, calcitonin receptor, Bos taurus-like neuronal axonal protein, FRA-2, a polypeptide similar to human oxygen-regulated protein, a polypeptide similar to mouse mrg 1 protein, pentraxin, olfactomedin-related protein, arc-growth factor enriched in dendrites, protein tyrosine phosphatase, melanocortin 4 receptor, ALK-7 kinase, neuritin and CB1 cannabinoid receptor.

53. The method of claim 52, wherein the at least one gene encodes a polypeptide selected from the group consisting of GABA-B receptor subunit gb2, FRA-2 and CB1 cannabinoid receptor.

54. The method of claim 49, wherein the at least one gene is identified in Table 2.

55. The method of claim 49, wherein the at least one gene is identified in Table 4.

56. The method of claim 55, wherein the at least one gene identified in Table 4 encodes a polypeptide selected from the group consisting of GABAB receptor 1d, tyrosine kinase receptor RET and Neurodap-1.

57. The method of claim 49, wherein the at least one gene is identified in Table 5.

58. The method of claim 57, wherein the at least one gene identified in Table 5 encodes a polypeptide selected from the group consisting of inhibin alpha-subunit and vesicular transport factor.

59. The method of claim 49, wherein the at least one gene is identified in Table 6.

60. The method of claim 59, wherein the at least one gene identified in Table 6 encodes a polypeptide selected from the group consisting of GABAB receptor 1c and phosphatidylinositol 4-kinase.

61. The method of claim 49, wherein the at least one gene is identified in Table 7.

62. The method of claim 61, wherein the at least one gene identified in Table 7 encodes a polypeptide selected from the group consisting of somatostatin-14 and kainate receptor subunit (ka2).

63. The method of claim 49, wherein the at least one gene is identified in Table 8.

64. The method of claim 63, wherein the at least one gene identified in Table 8 encodes a polypeptide selected from the group consisting of melanocortin-3

receptor, somatostatin, metabotropic glutamate receptor 3, NCAM polypeptide and synaptic SAPAP-interacting protein.

65. The method of claim 49, wherein the at least one gene is identified in Table 9.

66. The method of claim 65, wherein the at least one gene identified in Table 9 encodes calpastatin.

67. The method of claim 49, wherein the at least one gene is identified in Table 10.

68. The method of claim 67, wherein the at least one gene identified in Table 10 encodes a polypeptide selected from the group consisting of RAC protein kinase alpha, alpha-2B-adrenergic receptor and SNAP-25A.

69. The method of claim 49, wherein the at least one gene is identified in Table 11.

70. The method of claim 69, wherein the at least one gene identified in Table 11 encodes a polypeptide selected from the group consisting of oxytocin/neurophysin, NMDAR2C and GABA-A receptor epsilon.

71. The method of claim 49, wherein the at least one gene is identified in Table 12.

72. The method of claim 71, wherein the at least one gene identified in Table 12 encodes a polypeptide selected from the group consisting of phosphodiesterase I, tyrosine phosphatase and dopamine transporter.

73. The method of claim 49, wherein the at least one gene is identified in Table 13.

74. The method of claim 73, wherein the at least one gene identified in Table 13 encodes synaptotagmin IV homolog.

75. The method of claim 49, wherein the at least one gene is identified in Table 14.

76. The method of claim 75, wherein the at least one gene identified in Table 14 encodes a polypeptide selected from the group consisting of calmodulin, protein kinase rMNK2, phospholipase C-beta1b.

77. The method of claim 49, wherein the at least one gene is identified in Table 15.

78. The method of claim 77, wherein the at least one gene identified in Table 15 encodes a polypeptide selected from the group consisting of phosphatidylinositol 4-kinase and protein-tyrosine-phosphatase.

79. The method of claim 49, wherein the cocaine addiction-related behavior is cocaine craving.

80. The method of claim 49, wherein the level of expression of the gene is determined by detecting the level of expression of a protein encoded by the gene.

81. The method of claim 80, wherein the level of expression of the protein encoded by the gene is detected through western blotting by utilizing a labeled probe specific for the protein.

82. The method of claim 81, wherein the labeled probe is an antibody.

83. The method of claim 82, wherein the antibody is a monoclonal antibody.

84. The method of claim 49, wherein the level of expression of at least two or more genes in the sample is detected in (b).

85. The method of claim 49, wherein the level of expression of the gene is determined by detecting the level of expression of a mRNA corresponding to the gene.

86. The method of claim 85, wherein the level of expression of mRNA is detected by techniques selected from the group consisting of Northern blot analysis, reverse transcription PCR, real time quantitative PCR and microarray analysis.

87. The method of claim 49, wherein the agent is selected from the group consisting of antisense nucleotides, ribozymes and double-stranded RNAs.

88. A method for identifying an agent to be tested for an ability to prevent or inhibit cocaine addiction-related behavior, the method comprising:

- a) contacting a brain tissue sample from each of a subject having a cocaine addiction-related behavior and a cocaine addiction-free subject;
- b) detecting a level of expression of at least one gene in both tissue samples, wherein the gene encodes a polypeptide selected from the group consisting of hypertension-regulated vascular factor, myelin-associated basic protein, PB cadherin, calcitonin receptor, melanocortin 4 receptor, ALK-7 kinase and retroposon.
- c) subtracting the level of expression of the gene in the sample obtained from the cocaine addiction-free subject from the level of expression of the gene in the sample obtained from the subject having cocaine addiction-related behavior to provide a first value;
- d) administering a candidate agent to each of a subject having a cocaine addiction-related behavior and a cocaine addiction-free subject;
- e) detecting a level of expression of at least one gene in both tissue samples obtained from the subjects treated with the candidate agent;
- f) subtracting the level of expression of the at least one gene in the sample obtained from the treated cocaine addiction-free subject from the level of expression of the gene in the sample obtained from the treated subject having the cocaine addiction-related behavior to provide a second value; and

g) comparing the second value with the first value wherein a decreased second value relative to the first value is indicative of an agent to be tested for an ability to prevent or inhibit cocaine addiction-related behavior.

89. A method for identifying agents to be tested for an ability to prevent or inhibit cocaine addiction-related behavior, the method comprising:

a) obtaining a brain tissue sample from each of a subject having a cocaine addiction-related behavior and a cocaine addiction-free subject;

b) detecting a level of expression of at least one gene in both tissue samples, wherein the gene encodes a polypeptide selected from the group consisting of GABA-B receptor subunit gb2, cell adhesion-like molecule, bos taurus-like neuronal axonal protein, similar to mouse chemokine-like factor, FRA-2, a polypeptide similar to human oxygen-regulated protein, a polypeptide similar to mouse mrg1 protein, pentraxin, malic enzyme, olfactomedin-related protein, arc-growth factor enriched in dendrites, protein tyrosine phosphatase, krox, neuritin, microtubule-associated protein 2d and CB1 cannabinoid receptor;

c) subtracting the level of expression of the gene in the sample obtained from the cocaine addiction-free subject from the level of expression of the gene of the sample obtained from the subject having cocaine addiction-related behavior to provide a first value;

d) administering a candidate agent to each of a subject having a cocaine addiction-related behavior and a cocaine addiction-free subject;

e) detecting a level of expression of the gene in both tissue samples obtained from the subjects treated with the candidate agent;

f) subtracting the level of expression of the gene in the sample obtained from the treated cocaine addiction-free subject from the level of expression of the gene in the sample obtained from the treated subject having the cocaine addiction-related behavior to provide a second value; and

g) comparing the second value with the first value wherein an increased second value relative to the first value is indicative of an agent to be tested for an ability to prevent or inhibit cocaine addiction related behavior.